

What is claimed is:

CLAIMS

1. A polypeptide comprising an amino acid sequence encoding an EGF-like domain, wherein the amino acid sequence has the binding characteristics of NRG3.
2. The polypeptide of claim 1 wherein the binding characteristics of NRG3 comprise
  - (a) binding to ErbB4 receptor but not to ErbB2 receptor or ErbB3 receptor under experimentally comparable conditions; and
  - (b) activation of ErbB4 receptor tyrosine phosphorylation.
3. The polypeptide of claim 1 wherein the amino acid sequence has at least 75% amino acid sequence homology to the amino acid sequence SEQ ID NO:4.
4. The polypeptide of claim 1, wherein the polypeptide binds to the ErbB4 receptor and stimulates tyrosine phosphorylation of the ErbB4 receptor.
5. A polypeptide that binds ErbB4 receptor, which polypeptide is selected from the group consisting of
  - (a) a polypeptide comprising an amino acid sequence having at least 75% sequence homology to the extracellular domain NRG3 (SEQ ID NO:3 or 7).
  - (b) a polypeptide comprising an amino acid sequence having at least 75% sequence homology to SEQ ID NO:2 or SEQ ID NO:6;
  - (c) a further mammalian homologue of polypeptide (a) or (b);
  - (d) a soluble form of any of the polypeptides (a) - (c) having a transmembrane domain that cannot anchor the polypeptide in a cell membrane; and
  - (e) a derivative of any of the polypeptides (a) - (d) having the binding characteristics of NRG3.

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6. The polypeptide of claim 1 encoded by a NRG3 nucleic acid open reading frame sequence in ATCC deposit 209156 (pLXSN.mNRG3).
  7. The polypeptide of claim 1 encoded by a NRG3 nucleic acid open reading frame sequence in ATCC deposit 209157 (pRK5.tk.neo.hNRG3B1).
  8. The polypeptide of claim 1 encoded by a NRG3 nucleic acid open reading frame sequence in ATCC deposit 209297 (pRK5.tk.neo.hNRG3B2).
  9. The polypeptide of claim 1 which is devoid of a cytoplasmic domain, or devoid of a transmembrane domain that can anchor the polypeptide in a cell membrane, or both.
  10. The polypeptide of claim 1 unaccompanied by native glycosylation.
  11. The polypeptide of claim 1 which has a variant glycosylation.
  12. An antagonist of the polypeptide of claim 1.
  13. An agonist of the polypeptide of claim 1.
  14. An isolated nucleic acid molecule encoding the polypeptide of claim 1.
  15. The nucleic acid molecule of claim 14 further encoding the extracellular domain of a mammalian NRG3.
  16. The nucleic acid molecule of claim 15, wherein the encoded extracellular domain has at least 75% amino acid sequence identity to the amino acid sequence of SEQ ID NO:3 or

SEQ ID NO:7.

17. The nucleic acid molecule of claim 14 wherein the encoded amino acid sequence is devoid of a cytoplasmic domain or a transmembrane domain that can anchor the polypeptide in a cell membrane, or both.

18. An expression vector comprising the nucleic acid molecule of claim 14 operably linked to control sequences recognized by a host cell transformed with the vector.

19. An expression vector according to claim 18 obtainable as ATCC 209156 (pLXSN.mNRG3).

20. An expression vector according to claim 18 obtainable as ATCC 209157 (pRK5.tk.neo.hNRG3B1).

21. An expression vector according to claim 18 obtainable as ATCC 209297 (pRK5.tk.neo.hNRG3B2).

22. A host cell comprising the vector of claim 18.

23. The host cell of claim 22 which is a mammalian cell.

24. The host cell of claim 23 which is a Chinese hamster ovary cell line.

25. A method for producing the amino acid sequence encoding an EGF-like domain that binds ErbB4 receptor, the method comprising:

a) culturing a cell comprising the nucleic acid of claim 14; and

b) recovering the polypeptide from the cell culture.

26. The method of claim 25 wherein the polypeptide is secreted into the culture medium and recovered from the culture medium.

27. An antibody that specifically binds to the polypeptide of claim 1.

28. A hybridoma cell line producing the antibody of claim 27.

29. An immunoadhesin comprising the polypeptide of claim 1 fused to an immunoglobulin sequence.

30. The immunoadhesin of claim 29, further comprising the EGF-like domain of SEQ ID NO:4.

31. The immunoadhesin of claim 29 wherein the immunoglobulin sequence is an immunoglobulin heavy chain constant domain sequence.

32. The immunoadhesin of claim 31 wherein the immunoglobulin sequence is a constant domain sequence of an IgG-1, IgG-2 or IgG-3.

33. A method of detecting an NRG3 in a sample, the method comprising:  
a) contacting the antibody of claim 27 with the sample;  
b) detecting binding of the antibody to a polypeptide in the sample, wherein the polypeptide is an NRG3.

34. A method of detecting ErbB4 receptor in a sample, the method comprising:

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- a) contacting the polypeptide of claim 1 with the sample; and
  - b) detecting binding of the amino acid sequence to a protein in the sample.
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35. The method of claim 34 wherein the sample comprises a cell expressing ErbB4 receptor on its surface.

36. The method of claim 35 wherein the sample is a mammalian tissue sample.

37. A method of administering a NRG3 polypeptide to a mammal experiencing a disorder treatable with NRG3,  
wherein the method comprises introducing into the mammal a cell comprising the nucleic acid of claim 14, and  
wherein the NRG3 polypeptide is secreted by the cell.

38. The method of claim 37 wherein the cell is contained within a porous matrix and the matrix is administered to the mammal.

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